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Evaluation of anthropometric parameters, Liver Enzymes, Albumin, and Lipid Profile Levels in Patients with Type Two Diabetes Mellitus, in Amran City, Yemen

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Abstract

Background: Type 2 diabetes mellitus (T2DM), which accounts for 90–95% of diabetes cases, is characterized by chronic hyperglycemia resulting from insulin resistance or deficiency. The liver plays a central role in regulating glucose levels, and hepatic insulin resistance in T2DM contributes to hyperglycemia. This imbalance can lead to an accumulation of fat in the liver, increasing the risk of nonalcoholic fatty liver disease (NAFLD) and its progression to nonalcoholic steatohepatitis (NASH). **Objective:** This study aimed to evaluate anthropometric parameters, liver enzymes, albumin levels, and lipid profiles (total cholesterol and triglycerides) in patients with T2DM in Amran City, Yemen. **Results:** Patients with T2DM showed significant increases in mean body mass index (BMI) (27.26±4.42; P<0.001), diastolic blood pressure (BP) (81.08±10.41; P≤0.004), systolic BP (128.79±19.75; P≤0.001), alkaline phosphatase (ALP) (198.08±58.37; P<0.001), triglycerides (198.94±91.94; P<0.001), total cholesterol (204.63±39.84; P=0.011), and fasting blood sugar (FBS) (178.58±80.23; P<0.001). Additionally, a significant decrease in albumin levels (4.09±0.37; P<0.001) was observed. No significant differences were found in alanine aminotransferase (ALT) (P=0.377), aspartate aminotransferase (AST) (P=0.897), and gamma-glutamyl transferase (GGT) (P=0.238). **Conclusion:** Patients with T2DM in Amran City exhibited elevated BMI, blood pressure, ALP, and lipid levels, particularly triglycerides, alongside reduced albumin levels. Notably, ALP was the most significantly altered liver enzyme, indicating a potential risk of liver dysfunction in these patients.

Keywords: Alkaline phosphatase (ALP), Alanine transaminase (ALT), Aspartate transaminase (AST), γ-Glutamyl transferase (GGT) and type 2 diabetes

ألملخص: الخلفية: يُمثّل داء السكري من النوع الثاني (T2DM) نسبت ٩٠–٩٥٪ من حالات السكري، ويتميّز بفرط سكر الدم المزمن نتيجة مقاومة الإنسولين أو نقصه. يلعب الكبد دورًا محوريًا في تنظيم الغلوكوز، وتؤدي مقاومة الإنسولين الكبدية في T2DM إلى اختلال هذا التوازن، مما يعزز تراكم الدهون في الكبد وزيادة خطر الإصابة بمرض الكبد الدهني غير الكحولي (NAFLD) وتطوره إلى التهاب الكبد الدهني غير الكحولي (NASH) **الهدف:** هدفت هذه الدراسة إلى تقييم المؤشرات الجسمانية، وإنزيمات الكبد، ومستويات الألبومين، والدهون (الكوليسترول الكلي والدهون الثلاثية) لدى مرضى السكري من النوع الثاني في مدينة عمران، اليمن. **النتائج:** أظهرت الدراسة أن مرضى السكري من النوع الثاني يعانون من زيادات معنوية في متوسط مؤشر كتلة الجسم (٢٧.٢٦±٤.٤٢؛ P<0.001)، ضغط الدم الانبساطي (٨١.٠٨±١٠.٤١؛ P≤0.004)، ضغط الدم الانقباضي (١٢٨.٧٩±١٩.٧٥؛ P≤0.001)، إنزيم ALP (198.08±58.37؛ P<0.001)، الدهون الثلاثية (١٩٨.٩٤±٩١.٩٤؛ P<0.001)، الكوليسترول الكلي (٢٠٤.٦٣±٣٩.٨٤؛ P=0.011)، وسكر الدم الصائم (١٧٨.٥٨±٨٠.٢٣؛ P<0.001). كما سُجّل انخفاض معنوي في مستوى الألبومين (٤.٠٩±٠.٣٧؛ P<0.001). ولم تُسجل

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فروق معنوية في إنزيمات ALT (P=0.377)، و AST (P=0.897)، و GGT (P=0.238). **الاستنتاج:** أظهر مرضى السكري من النوع الثاني في مدينة عمران ارتفاعًا في مؤشر كتلة الجسم، وضغط الدم، ومستويات إنزيم ALP والدهون، خصوصًا الدهون الثلاثية، إلى جانب انخفاض في مستويات الألبومين. وكان إنزيم ALP هو الأكثر تأثرًا بين إنزيمات الكبد، مما يشير إلى وجود خطر محتمل للإصابة باضطرابات في وظائف الكبد لدى هؤلاء المرضى.

1. INTRODUCTION

Diabetes Mellitus (DM) refers to a group of metabolic disorders marked by elevated blood glucose levels resulting from defects in insulin secretion, insulin action, or a combination of both. [1] Diabetes mellitus (DM) is characterized by elevated levels of glucose in the bloodstream (hyperglycemia), excessive appetite (polydipsia), and excessive hunger (Polyphagia) [2]. Diabetes is a widespread metabolic disorder that is experiencing a significant global increase in prevalence [3].
Persons diagnosed with Type 2 Diabetes (T2D) exhibit a higher propensity for abnormalities in liver function tests compared to persons without diabetes who are in good condition [4]. The association between type 2 diabetes (T2D) and several liver illnesses, such as nonalcoholic, Cirrhosis, and hepatocellular carcinoma, has been established in epidemiological research. Liver problems are widely recognized as a significant contributor to death in individuals with type 2 diabetes[5].
Nonalcoholic fatty liver disease (NAFLD) is a liver disorder characterized by excessive lipid accumulation within hepatocytes in the absence of significant alcohol consumption. Nonalcoholic steatohepatitis (NASH) is characterized by hepatocellular destruction and concurrent inflammation of the portal vein and lobules in up to 40% of patients [5].
Diabetic Dyslipidemia (DD) is a widespread macrovascular issue associated with patients with Diabetes Type 2 (T2D). In both industrialized and developing countries, diabetes type 2 is well recognized as a significant health issue and a prominent risk factor for cardiovascular disease (CVD) [6].
There are many studies on liver enzymes and incident diabetes mellitus type two risk [7-12]. Therefore, in our study, subjects with diabetes exhibited higher liver enzymes and lipid profile levels than those without T2D. The most prevalent deviation in liver enzymes was seen in the case of ALP. However, other enzymes did not rise significantly in people with diabetes. The most lipid abnormalities in patients with diabetes are triglycerides. There is a positive correlation between patients with Diabetes Type 2 (T2D) in Amran City – Yemen, with a higher risk of developing elevated ALP levels, total Cholesterol, Triglyceride, and decreased Albumin levels.

2. MATERIALS AND METHODS:

2.1. Study design and subjects selection

This case-control study was conducted on patients of T2DM in Amran City through the period from November 2023 to March 2024. Based on a personal interview with patients and obtaining written consent from them. The study includes a total of sample 120 individuals of both sexes (57 males and 63 females), aged between 20 to 80 years, and subdivided into 80 individuals who have type 2 Diabetes (36 males and 44 females) and 40 non-diabetic healthy individuals control (21 males and 19 females) subjects. The patients were selected randomly by publishing posters in Amran city.

2.2. Blood sampling

The participants fasted for at least 10 hours before providing the blood sample. Then, about 5 ml of venous blood was collected from subjects through a venous puncture in anticoagulant-free tubes. The samples were sent to the biochemistry section immediately. The serum was separated by centrifugation at 4000 rpm for five minutes.

2.3. Biochemical analysis

The samples were analyzed immediately by a chemical auto-analyzer (biobased bk 200) for the estimate of FBS, to assess the diabetic state, ALT, AST, ALP, GGT, and Albumin to assess liver function, Triglyceride, and Cholesterol to assess lipids in subjects on the chemical instrument.

3.4. Inclusion and Exclusion Criteria

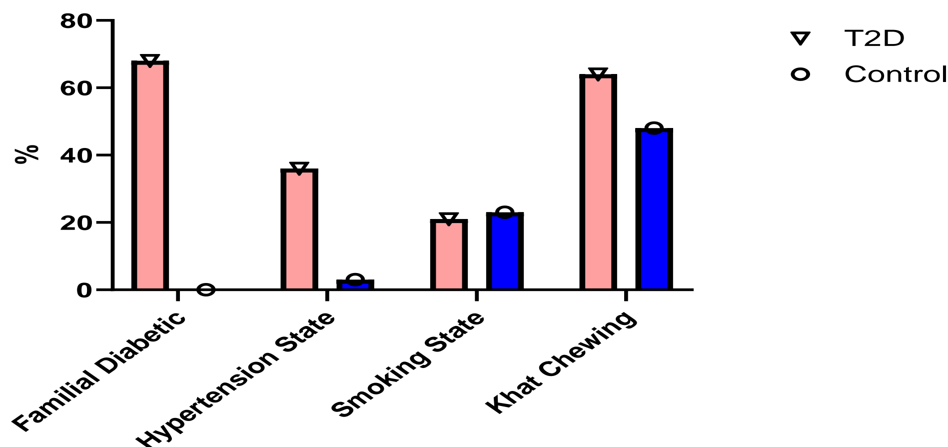
We included the patients previously diagnosed with type 2 diabetes mellitus with FBS >126 mg/dl, according to WHO. The control group with no diabetes and FBS of less than 126 mg/dl are included in the study. We excluded participants who had a history of some disease that affects the liver, such as (hepatitis B and C, liver cirrhosis, hepatocarcinoma, alcoholism, severe hemolytic anemia, and sub-clinical hypothyroidism). Also, control participants with FBS of more than 126 mg/dl were excluded.

3.5. statistical analysis

SPSS Version 24 was used to do the statistical analysis of the data. The mean ± standard deviation (SD) communicates quantitative data, while frequencies (%) express qualitative variables. The correlation between liver markers and diabetes type 2 (T2D) was evaluated using Pearson's correlation coefficient test. An independent sample t-test examined anthropometric and diabetes type 2 (T2D) differences between the gender and case-control groups. The study employed multinomial logistic regression analysis to assess the associations between liver enzymes and type 2 diabetes (T2D). Results with a P-value below 0.05 or 0.01 are considered statistically significant.

1. RESULT:

One hundred twenty participants (80 confirmed T2DM and 40 controls) were enrolled in this study. From the T2DM group, males are 36 (45%), and females are 44 (55%). At the same time, the control group contains 21 males (52.5%) and 19 females (47.5%). The mean ages of the T2DM participants were 51.33±11.98, and the control participants were 41.53±11.34. This study showed that participants who have familial diabetes from a T2DM group were 54 (67.5%). The participants with hypertension disease from a T2DM group were 29 (36.3%), and from the control group was only one (2.5%). In the group with diabetes who smoked and chewed Khat were 17 (21.3%) and 51 (63.8%), respectively, while those who smoked and chewed Khat from the control group were 9 (22.5%) and 19 (47.5%), respectively (Fig 1).



□ **Fig 1: The essential characteristics of the study subjects.**

This study found that T2D patients had significantly increased mean value BMI of 27.26±4.42 ($P < 0.001$), diastolic BP mean 81.08±10.41 ($P \leq 0.004$), systolic BP mean 128.79±19.75 ($P < 0.001$) compared to healthy control subjects (Fig 2).

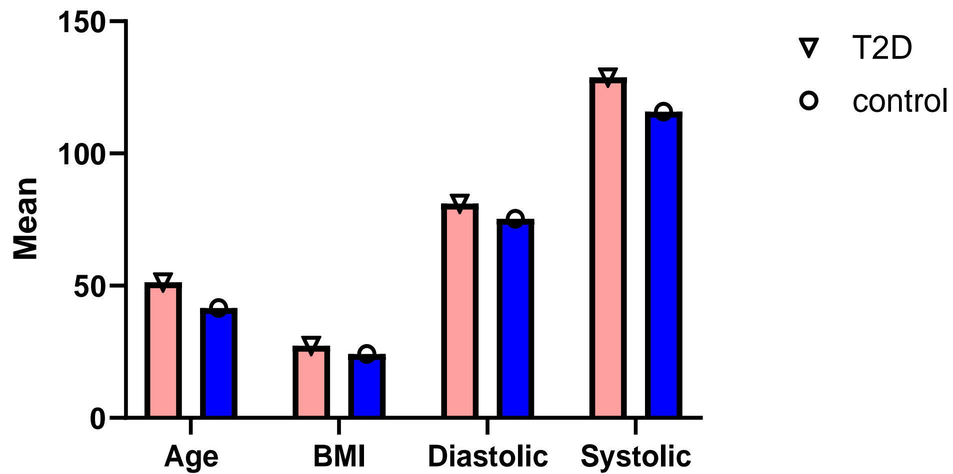


 Fig 2: Anthropometric data of healthy controls and T2DM patients.

Descriptive statistics of biochemical data of the study population in (Fig 3,٤) showed that the result shows an increase in ALT in 10% of patients and 10% of control, increase AST in 3.75% of patients and 5% of control, increase ALP in 92.5% of patients and 55% of control, increase GGT in 16.25% of patients and 15% of control. And showed an increase in Triglyceride in 68.75% of patients and 25% of control, an increase in Cholesterol in 52.5% of patients and 22.5% of control, increase in 77.5% of patients and 7.5% of control above the normal ranges. Also, the results show decreases the albumin in 7.5% of patients and no decrease in control lower than normal range.

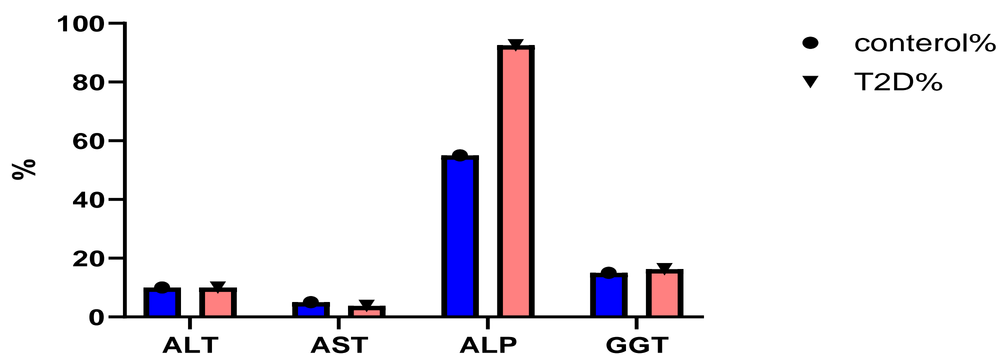


Fig 3 :Prevalence of elevated liver enzymes above the normal ranges in patients and control group.

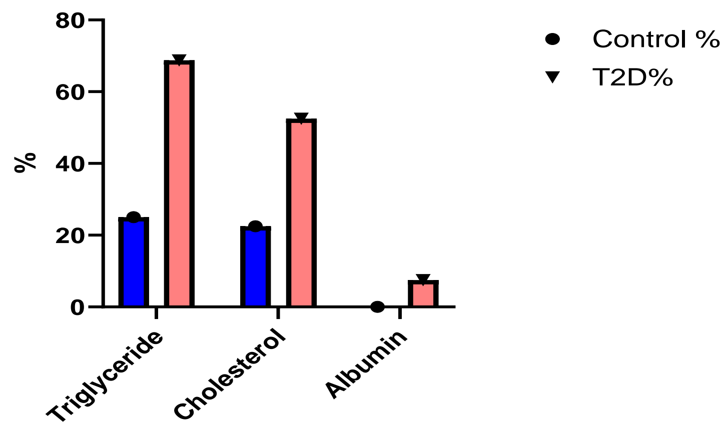


Fig 4:Prevalence of elevation of Triglyceride, Cholesterol and decreases Albumin from the normal range in diabetic and control group.

From (table 1), for every unit that increased the ALP score, it was observed that participants who had Hypertension and T2D were more likely to increase ALP by 1.010 times than those who had no hypertension, holding all other independent variables constant (P-value< 0.05). For every unit increase in ALP score, it observed that participants who were smoking and T2D were more likely to increase ALP by 1.014 times than others, holding all other independent variables constant (P-value< 0.05). For every one-unit increase in ALT score, It was observed that participants who were smoking and T2D were more likely to increase ALT by 1.097 times than others, holding all other independent variables constant (P-value< 0.05). For every unit that increased in AST score, it was observed that participants who were chewing Khat and T2D were less likely to decrease in AST by 0.932 times than others, holding all other independent variables constant (P-value< 0.05).

- Table 1: Logistic Regression results to study the effect of Hypertension, smoking, and chewing khat on liver enzymes on T2DM.

ID		Hypertension (Yes/No) (DV)			Smoking (Yes/No) (DV)			Chewing Khat (Yes/No) (DV)	
	B	Exp(B)	P-value	B	Exp(B)	P-value	B	Exp(B)	P-value
ALT	0.017	1.017	0.519	0.092	1.097**	0.006	0.051	1.052	0.072
AST	-0.047	0.954	0.234	-0.069	0.933	0.150	-0.070	0.932*	0.042
ALP	0.010	1.010*	0.032	0.014	1.014*	0.012	0.007	1.007	0.113
GGT	-0.012	0.989	0.426	-0.010	0.990	0.589	0.003	1.003	0.835

3. DISCUSSION

This study revealed the individuals diagnosed with Type 2 Diabetes (T2D) had a considerably greater average age in comparison to the group without diabetes. This result is consistent with a study conducted by Schellenberg E. et al. and Nwarfor A. et al., which show that a significant proportion of individuals aged 45 years and above in developing nations are affected by diabetes [13, 14]. This finding clarifies why abnormalities in glucose metabolism and a decline in energy homeostasis accompany aging in the human body. The two most important factors contributing to hyperglycemia

are believed to be increasing insulin resistance and a shortage of insulin secretion that occurs with aging [15]. Our investigation found a substantial rise in BMI in T2D patients compared to healthy control subjects. These findings are consistent with the studies conducted by Bellou V et al., Hillier T.A et al., and Dahman LSB et al. [16, 17]. Increased anabolic activity is one way that diabetes patients can acquire more weight; because T2DM patients have higher insulin levels, this hormone functions as an anabolic hormone, promoting protein synthesis and lipogenesis while decreasing protein catabolism. Another mechanism for weight gain is insulin resistance; the patient's cells cannot utilize the glucose; therefore, polyphagia occurs and leads to weight gain [18]. Further research exploring the similarly significant rise in systolic and diastolic BP in T2D patients compared to healthy control subjects. These findings are consistent with the study conducted by Botas M et al., Dahman LSB et al., and Yao X et al.[19-21]. Patients with diabetes mellitus have higher peripheral arterial resistance as a result of vascular remodeling, and they also have higher body fluid volume because of hyperinsulinemia and hyperglycemia brought on by insulin resistance. These two methods both result in higher systemic blood pressure[22].

The present study shows a significant increase in total Cholesterol and triglycerides in a person with diabetes compared with a group without diabetes individuals; these results are consistent with previous studies conducted by Kumar A. et al. and Albertus J et al.[12, 23]. At the same time, elevated Cholesterol is inconsistent with the study by Mohamed R et al. [24]. Elevation of lipid profile in diabetic patients due to hyperglycemia and elevated insulin resistance have various impacts on fat metabolism, leading to the development of atherogenic dyslipidemia, and the abnormalities in triglycerides and cholesterol levels define this dyslipidemia. Very low-density lipoprotein (VLDL) cholesterol is believed to be overproduced as a result of hyperinsulinemia and the central obesity that frequently accompanies insulin resistance. Triglyceride-rich particles increase, HDL particles decrease, and small-density LDL particles result [25]. The disruption of the regular mechanism involved in producing and removing triglycerides can lead to fibrosis, Cirrhosis, and hepatocellular cancer [26, 27]. In addition, triglycerides are valuable lipids accumulated in the liver of individuals with nonalcoholic fatty liver disease (NAFLD). Moreover, there is no statistically significant difference in ALT and AST levels among patients with type 2 diabetes mellitus (T2DM) when compared to a healthy control group. These results differ from previous studies conducted by Mathur S et al., Shibabaw T et al., Ghimire S et al., and Islam S et al. [7, 28-30]. In the investigation we conducted, the significant difference in ALP level between the person with diabetes group and the group without diabetes is consistent with studies performed by Mathur S et al., Ghimire S et al., Sunitha S et al., Eltayeb A. et al. and Abbas I. [7, 9, 29, 31, 32]. While inconsistent with Shibabaw T et al. and Azeez et al. [8, 33]. The presence of ALP in the liver has been observed to be linked to the cell membrane, which is next to the biliary canaliculus. Elevated levels of this liver isoenzyme in the bloodstream suggest cholestasis rather than mere liver cell injury[7]. The potential reason for the elevation of ALP levels in the absence of ALT and AST is that ALP is an isoenzyme present in adipose tissue. Diabetes can lead to abnormalities in adipose tissue and obesity, increasing blood ALP levels. In this investigation, we observed a positive association between ALP and BMI, which aligns with the findings of a prior study conducted by Khan AR et al.[34]. Additionally a substantial decrease in albumin levels in patients with type 2 diabetes mellitus (T2DM) compared to the group without diabetes subjects. This finding is consistent with a recent study by Ghimire S et al.[29]. Albumin is an indicator of the liver's synthetic function when finding the effect of diabetes on the liver.

When studying the association between type 2 diabetes mellitus variables and liver enzymes to determine the potential impact of these variables on the concentration of hepatic markers. Our study indicates favorable associations between ALP, FBG, triglycerides, BMI, and diastolic blood pressure. Furthermore, the current investigation demonstrated a favorable association between ALT, AST, and triglycerides. A correlation has been observed between GGT and AST, ALT, ALP, and triglycerides. Furthermore, a negative association has been observed between albumin levels and FBS, ALP, SBP, and Age. Previous studies have demonstrated a favorable correlation between liver enzymes and blood lipid profile in persons with type 2 diabetes (T2D) [20, 35, 36]. This finding provides evidence for the involvement of hepatic insulin resistance in the development of nonalcoholic fatty liver disease (NAFLD) in persons with type 2 diabetes[37, 38].

The current investigation found a significant correlation between serum ALP levels and Hypertension in people with diabetes. In a recent study conducted by Shimizu Y et al., it was found that ALP could serve as an indication of Hypertension in the Japanese population [39]. The independent connection between blood ALP levels and Hypertension in persons with diabetes in Amran City lacks a straightforward explanation. It is conceivable that persons with Hypertension may develop nonalcoholic fatty liver disease (NAFLD) over an extended duration of increased blood pressure [40]. On the other hand, there demonstrates a positive correlation between smoking habits and elevated ALP and ALT blood levels, which aligns with the findings reported by Salem K et al. [41]. Cigarette smoke perpetuates lipid peroxidation, resulting in detrimental effects on the liver's biological cell membrane. Additionally, serum aminotransferases exhibit heightened sensitivity in detecting hepatocellular damage. Smokers, unlike nonsmokers, experience elevated levels of ALT and ALT due to the leakage of enzymes into their bloodstream.

Moreover, our investigation has identified a correlation between smoking and unusually high levels of the liver enzyme AST in diabetic individuals who chew Khat. This conclusion corroborates the previous study conducted by Hegazy MAE et al. [42]. The underlying mechanism by which Khat induces an increase in liver enzymes remains uncertain and necessitates additional inquiry. Our study demonstrates a correlation between smoking and Hypertension. Specifically, smokers who have diabetes are more prone to developing Hypertension compared to nonsmokers with diabetes. These findings align with the research conducted by Kogoya D et al.[43].

4. **Conclusions:**

In this study, we found that individuals with Type 2 Diabetes Mellitus (T2DM) had significantly higher levels of body mass index (BMI), systolic blood pressure (BP), diastolic BP, liver enzymes, and lipid profiles compared to those without T2DM. The most notable change in liver enzymes was an increase in alkaline phosphatase (ALP). Other liver enzymes did not show significant increases, but their levels remained elevated compared to the control group, suggesting that diabetes impacts liver function.

Among lipid profiles, triglycerides were the most commonly elevated abnormality. We observed that increased ALP activity and decreased albumin levels were independently associated with T2DM in Amran City. Additionally, smoking was linked to elevated levels of alanine aminotransferase (ALT) and ALP, while Khat chewing was associated with elevated aspartate aminotransferase (AST).

Our findings indicate a positive correlation between elevated ALP levels, decreased albumin levels, and an increased risk of developing T2DM in patients from Amran City. These biomarkers can help

predict the risk of liver diseases in individuals with T2DM, making regular monitoring of ALP and albumin levels advisable for early detection of potential complications.

Finally, we recommend conducting further research in underdeveloped nations to better understand the role of liver enzymes in T2DM and to inform public health strategies tailored to these populations.

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